CHAPTER 3
SECTION 6.1

HIGH DOSE CHEMOTHERAPY AND STEM CELL TRANSPLANTATION

Issue Date: November 1, 1983
Authority: 32 CFR 199.4(e)(5) and (g)(15)

I. PROCEDURE CODES

38230, 38240, 38241, 88240, 88241

II. DESCRIPTION

A. High dose chemotherapy (HDC) is defined as the use of cytotoxic therapeutic agents (that are otherwise approved by the FDA for general use in humans) in dosages and/or frequencies of dosage that exceed the FDA labelling for the agent. HDC is generally considered when conventional regimens of chemotherapeutic agents have failed to arrest disease progression. One of the major adverse effects of HDC is that of bone marrow suppression, itself a potentially lethal process.

B. Stem cell "transplantation" or "rescue" is defined as a technique for collecting stem cells from a donor (either from the bone marrow or from the bloodstream), preparing and storing the collected stem cells, then reinfusing the prepared stem cells into the bloodstream of a patient in the treatment of oncologic, hematologic or lymphoproliferative disease with curative potential. The goal of stem cell "transplantation" or "rescue" is to reverse the bone marrow suppression caused by either HDC or by a primary bone marrow disease process (e.g., aplastic anemia).

There are four general types of stem cell "transplantation" or "rescue":

1. Autologous bone marrow transplant (ABMT), where the patient is both donor and recipient of stem cells harvested from the bone marrow.

2. Peripheral stem cell therapy (PSCT), where the patient is both donor and receipient of stem cells harvested from the bloodstream using the apheresis process.

3. Allogeneic bone marrow transplantation (BMT), where stem cells from a histocompatible donor (other than the patient) are harvested, then later infused into the bloodstream of the patient. With BMT, the patient may have either a related or unrelated donor who has the same or closely matched human leukocyte antigen (HLA) typing necessary for successful transplantation.

4. Umbilical cord blood stem cell transplantation (UCBT), where stem cells are harvested from the umbilical cord and placenta, then later infused into the bloodstream of the patient.

III. POLICY

A. Benefits are allowed for HDC with ABMT or PSCT.

1. TRICARE Prime enrollee must have a referral from his/her Primary Care Manager (PCM) and an authorization from the Health Care Finder (HCF) before obtaining transplant-related services. If network providers furnish transplant-related services without prior PCM referral and HCF authorization, penalties will be administered according TRICARE network provider agreements. If Prime enrollees receive transplant-related services from non-network civilian reporters without the required PCM referral and HCF authorization, Managed Care Support (MCS) contractors shall reimburse charges for the services on a Point of Services basis. Special cost-sharing requirements apply to Point of Service claims.

2. For Standard and Extra patients residing in a Managed Care Support (MCS) region, preauthorization authority is the responsibility of the MCS Medical Director, Health Care Finder, or other designated utilization staff.

B. Allogeneic Stem Cell Transplantation (Allogeneic Bone Marrow Transplantation).

The Air Force Wilford Hall Medical Center (WHMC), Lackland AFB, Texas, is designated the national Specialized Treatment Service Facility (STSF) for allogeneic bone marrow transplantation and umbilical cord blood transplantation.

1. For admissions on or after October 1, 1997, all beneficiaries who reside in the continental United States (i.e., 48 contiguous states and the District of Columbia) and are in need of an allogeneic stem cell transplantation, must be evaluated by WHMC before receiving an allogeneic stem cell transplantation (with or without HDC), except for those beneficiaries participating in DoD's cancer demonstration project.

2. If the allogeneic stem cell transplantation cannot be performed at WHMC an STSF NAS will be issued by WHMC.

NOTE: An STS NAS is not required for TRICARE Prime enrollees even when these beneficiaries use the Point of Service (POS) option. The enrollees are required to obtain authorization from the Health Care Finder.

C. The designated preauthorizing authority shall only use the criteria contained in this policy when preauthorizing HDC with ABMT or PSCT (with or without HDC), and allogeneic BMT (with or without HDC) and allogeneic UCBT (with or without HDC).

D. HDC with ABMT or PSCT is covered in the treatment of the following malignancies:

1. Non-Hodgkin's lymphoma, intermediate or high grade; and Hodgkin's disease when:

a. Conventional dose chemotherapy has failed; or

b. The patient has relapsed following a course of radiation therapy, and has also failed at least one course of conventional dose chemotherapy subsequent to the failed radiation therapy; and

c. In the case of ABMT, the patient has adequate marrow function and no evidence of marrow involvement with lymphoma.

NOTE: For purposes of coverage, mantle cell lymphomas will be considered as intermediate grade, non-Hodgkin's lymphomas.

2. Neuroblastoma, Stage III or IV, when the patient is one for whom further treatment with a conventional dose therapy is not likely to achieve a durable remission.

3. Acute lymphocytic or nonlymphocytic leukemias (e.g., myelocytic, myelogenous, myeloblastic, or myelomonoblastic);

4. Primitive neuroectodermal tumors (PNET)/Ewing's Sarcoma.

5. Gliofibromas (also known as desmoplastic astrocytoma; desmoplastic glioblastoma).

6. Glioblastoma multiforme.

7. Posterior fossa teratoid brain tumors.

8. Rhabdomyosarcoma and undifferentiated sarcomas.

9. Multiple myeloma.

10. Stage IV metastatic breast cancer or primary breast cancer that has spread to other sites of the body and that has relapsed after responding to first-line treatment; stage IV metastatic breast cancer or primary breast cancer that has spread to other sites of the body in patients who have not been previously treated with systemic therapy for metastatic disease; stage IV metastatic breast cancer or primary breast cancer that has spread to other sites of the body and that is responding to primary systemic therapy. This does not include primary breast cancer that has spread only to local lymph nodes. Breast cancer is considered a rare disease in men. Benefits may be allowed for male patients with stage IV metastatic breast cancer or primary breast cancer that has spread to other sites of the body subject to the same provisions as noted above.

11. Chronic myelogenous leukemia.

12. Waldenstrom's macroglobulinemia.

13. AL (Amyloid Light-Chain) Amyloidosis.

14. Wilms'tumor.

15. Trilateral retinoblastoma/pineoblastoma.

E. Allogeneic stem cell transplantation, with or without HDC, is covered in the treatment of the following disease processes when either a related or unrelated donor is used:

1. Aplastic anemia

2. Acute lymphocytic or nonlymphocytic leukemias (e.g., myelocytic, myelogenous, myeloblastic, myelomonoblastic); chronic myelogenous leukemia (CML); or preleukemic syndromes.

3. Severe combined immunodeficiency; e.g., adenosine deaminase deficiency and idiopathic deficiencies.

a. Partially matched-related donor stem cell transportation (without regard for the number of mismatched antigens in determining histocompatibility) in the treatment of Bare Lymphocyte Syndrome.

b. Unrelated donor and/or related donor (without regard for mismatched antigens) with or without T cell lymphocyte depletion in the treatment of familial erythrophagocytic lymphohistiocytosis, (FEL; generalized lymphohistiocytic infiltration; familial lymphohistiocytosis; familial reticuloendotheliosis; familial hemophagocytic lymphohistiocytosis; FHL) for patients whose medical records document failure of conventional therapy (etoposide; corticosteroids; intrathecal methotrexate; and cranial irradiation).

c. Partially matched-related donor stem cell transplantation (without regard for the number of mismatched antigens) in the treatment of X-linked severe combined immunodeficiency syndrome (X-Linked SCID).

4. Wiskott-Aldrich syndrome

5. Infantile malignant osteopetrosis (Albers-Schonberg syndrome or marble bone disease)

6. Thalassemia major

7. Intermediate and high grade lymphoma

8. Myeloproliferative/dysplastic syndromes

9. Congenital mucopolysaccharidoses

10. Congenital amegakaryocytic thrombocytopenia

11. Metachromatic leukodystrophy

12. Sickle cell disease

13. Chronic lymphocytic leukemia (CLL) when previous therapy has failed or when the CLL is refractory to conventional therapy.

14. Hyperosinophilic syndrome.

F. Unirradiated donor lymphocyte infusion (donor buffy coat infusion, donor leukocyte infusion or donor monomuclear cell infusion) is covered for patients with CML, who relapse following their first or subsequent course of HDC with allogeneic BMT. The medical record must document that the patient:

1. Is in relapse following an adequate trial of HDC with allogeneic BMT of CML; and

2. Qualified (or would have qualified) for authorization for HDC with allogeneic BMT according to the provisions set forth in this policy.

G. Allogeneic umbilical cord blood transplantation, with or without HDC, is covered for children and adolescents in the treatment of the following disease processes when either a related or unrelated donor is used. This list of conditions is not all inclusive, those conditions for which this procedure can be documented as medically necessary, appropriate and the standard of care may also be covered.

1. Aplastic anemia

2. Acute lymphocytic or non-lymphocytic leukemias

3. Chronic myelogenous leukemia

4. Severe combined immunodeficiency

5. Wiskott-Aldrich syndrome

6. Infantile malignant osteopetrosis

7. Blackfan-Diamond anemia

8. Fanconi anemia

9. Neuroblastoma

10. X-linked lymphoproliferative syndrome

11. Hunter syndrome

12. Hurler syndrome

13. Congenital amegakaryocytic thrombocytopenia

14. Sickle cell anemia

15. Globoid cell leukodystrophy

16. Adrenoleukodystrophy

17. Kostmann's syndrome

18. Lesch-Nyhan disease

19. Intermediate and high grade non-Hodgkin's Lymphoma.

20. Thalassemia major

21. Myelodysplastic syndrome

22. Non-Hodgkin's lymphoma

H. Syngeneic (identical twin donor) stem cell transplantation is covered for the treatment of Hodgkin's disease.

I. Review of WHMC Denials for allogeneic bone marrow and umbilical cord blood transplantation.

1. A denial of benefits issued by WHMC is not an initial determination as defined in 32 CFR 199, and is; therefore, not appealable through the TRICARE appeal process.

2. If the WHMC denial of benefits is overturned by the appropriate preauthorizing authority as outlined in paragraph III.A. above, written direction shall be provided to WHMC to issue appropriate authorization letter(s). Any written determination by the appropriate preauthorizing authority is considered to be an initial determination as defined in 32 CFR 199. In any case when the initial determination is adverse to the beneficiary or participating provider, the notice shall include a statement of the beneficiary's or provider's right to appeal the determination. The procedure for filing for an appeal also shall be explained.

3. WHMC does not provide authorizations for HDC with ABMT nor HDC with PSCT.

J. TRICARE will reimburse costs for donor searches.

1. Charges for donor searches must be fully itemized and billed by the transplant center.

2. Costs for donor searches will be cost-shared in accordance with established reimbursement guidelines for outpatient diagnostic testing.

3. Donor search costs may be billed at any time. There is no limit on how many searches a transplant center may request from the search printout.

K. For the purposes of TRICARE coverage, the greatest degree of incompatibility allowed between donor or recipient (for either related or unrelated donors) is a single antigen mismatch at the A, B, or Dr. locus except for:

1. Patients with undifferentiated leukemia, chronic myelogenous leukemia (CML), aplastic anemia, acute lymphocytic leukemia (ALL) or acute myelogenous leukemia (AML), when histocompatible related or unrelated donors are not available, a 3 antigen mismatch is allowed for related donors.

2. For patients under 18 years of age with a relapsed leukemia, when histocompatible related or unrelated donors are not available, parental CD34++ stem cell transplantation with 2-3 antigen mismatch is allowed.

L. Benefits will not be allowed for stem cell harvesting and/or cryopreservation and umbilical cord blood stem cell harvesting and/or cryopreservation until the stem cell reinfusion has been completed. In the event that the patient expires prior to the stem cell reinfusion being completed, benefits for the harvesting may be allowed.

M. Benefits are allowed for Hepatitis B and pneumococcal vaccines for patients undergoing transplantation.

N. Benefits may be allowed for DNA-HLA tissue typing in determining histocompatibility.

O. Charges for stem cell and umbilical cord blood preparation and storage shall be billed through the transplantation facility in the name of the TRICARE patient.

P. Charges for the umbilical cord blood bank may be allowed only for patients who have undergone a covered transplant.

Q. Claims for services and supplies related to the HDC and transplant for beneficiaries under the age of 18 will be reimbursed based on billed charges. Claims for HDC and transplant for adult patients, 18 years and older, will be reimbursed under the DRG payment system. Outpatient institutional facility charges will be paid as billed. Professional services are reimbursed under the CHAMPUS Maximum Allowable Charge Methodology.

R. Transportation of the patient by air ambulance may be cost-shared when determined to be medically necessary. Benefits for advanced life support air ambulance (to include attendant) may be preauthorized by the appropriate preauthorizing authority on an individual case basis in conjunction with the preauthorization for the services themselves.

S. In those cases where the beneficiary fails to obtain preauthorization, benefits may be extended if the services or supplies otherwise would qualify for benefits but for the failure to obtain preauthorization. If preauthorization is not received, the appropriate preauthorizing authority is responsible for determining if the patient meets the coverage criteria. Charges for transplant and transplant-related services provided to TRICARE Prime enrollees who failed to obtain PCM referral and HCF authorization for HDC with ABMT or PSCT will be reimbursed only under Point of Service rules.

IV. EXCEPTION

A demonstration project is being conducted wherein the DoD will participate in cancer treatment clinical trials under approved National Cancer Institute (NCI) protocols to include high dose chemotherapy with stem cell rescue (HDC/SCR). Refer to OPM, Chapter 23, Section 2 (TOM, Chapter 15) for additional information regarding the demonstration project.

V. EXCLUSIONS

Benefits will not be paid for:

A. HDC with ABMT or PSCT or HDC with allogeneic BMT if the patient has a concurrent condition (other existing illness) that would jeopardize the achievement of successful transplantation.

B. HDC with or without ABMT, HDC with or without PSCT, or HDC with or without allogeneic BMT if not specifically listed as covered in paragraph III.D., paragraph III.E. and paragraph III.G. under POLICY above.

C. In vitro stem cell processing (purging) as this procedure is considered unproven.

D. Expenses waived by the transplant center (i.e., beneficiary/sponsor not financially liable).

E. Services and supplies not provided in accordance with applicable program criteria (i.e., part of a grant, or research program; unproven procedure).

F. Administration of an unproven immunosuppressant drug that is not FDA approved.

G. Pre- or post-transplant nonmedical expenses (i.e., out-of-hospital living expenses, to include, hotel, meals, privately owned vehicle for the beneficiary or family members).

H. Transportation of a donor.

I. HDC with ABMT or PSCT is not a benefit for treatment of low grade non-Hodgkin's lymphoma. Allogeneic bone marrow transplantation for treatment of low grade non-Hodgkin's lymphoma is not a benefit.

J. Autologous umbilical cord blood transplantation therapy as this procedure is considered unproven.

K. Allogeneic peripheral stem cell transplantation for non-Hodgkin's lymphoma as this procedure is considered unproven.

L. Allogeneic bone marrow transplantation for neuroblastoma as this procedure is considered unproven.

M. Allogeneic donor bone marrow transplantation (infusion) performed with or after organ transplants for the purpose of increasing tolerance of the organ transplant is considered unproven.

N. HDC with ABMT or PSCT is not a benefit for treatment of desmoplastic small round-cell tumor.

O. HDC with ABMT or PSCT is not covered for treatment of non-metastatic breast cancer.

P. HDC with allogeneic BMT is not a benefit for treatment of Waldenstrom's macroglobulinemia.

Q. HDC with stem cell rescue is not a benefit for the treatment of ovarian cancer.

R. HDC with ABMT or PSCT is not a benefit for the treatment of yolk-sac tumor (endodermal sinus tumor).

S. HDC with allogeneic stem cell transplantation is not covered for the treatment of cold agglutinin disease.

T. Allogeneic BMT or PSCT with HDC is not covered for treatment of multiple myeloma.

U. HDC with allogeneic BMT is not covered for the treatment of Hodgkin's disease. This does not includes syngeneic stem cell transplantation which is covered for the treatment of Hodgkin's disease.

V. Donor lymphocyte infusion if not specifically listed as covered in paragraph III.F. under POLICY above.

VI. EFFECTIVE DATE

A. May 1, 1987, for HDC with ABMT or PSCT for Hodgkin's disease, non-Hodgkin's lymphoma and neuroblastoma.

B. November 1, 1987, for HDC with ABMT or PSCT for acute lymphocytic and nonlymphocytic leukemias.

C. November 1, 1983, for HDC with allogeneic bone marrow transplants using related donors.

D. July 1, 1989, for HDC with allogeneic bone marrow transplants using unrelated donors.

E. July 11, 1996, for HDC with ABMT or PSCT for multiple myeloma.

F. January 1, 1994, for HDC with ABMT and PSCT for Wilms' tumor.

G. October 1, 1995, for HDC with ABMT or PSCT for metastatic breast cancer.

H. August 1, 1996, for allogeneic umbilical cord blood transplants.

I. January 1, 1994, for HDC with ABMT or PSCT for chronic myelogenous leukemia.

J. January 1, 1996, for HDC with ABMT or PSCT for Waldenstrom's macroglobulinemia.

K. January 1, 1996, for allogeneic bone marrow transplants using related 3 antigen mismatch donors for patients with undifferentiated leukemia, chronic myelogenous leukemia (CML), aplastic anemia, acute lymphocytic leukemia (ALL) or acute myelogenous leukemia (AML).

L. October 1, 1996, for HDC with ABMT or PSCT for AL Amyloidosis.

M. January 1, 1995, for allogeneic bone marrow transplant for hypereosinophilic syndrome.

N. January 1, 1994, for HDC with ABMT or PSCT for Wilms' tumor.

O. May 1, 1997, for HDC with ABMT or PSCT for trilateral retinoblastoma/ pineoblastoma.

- END -